WHAT IS CLAIMED IS:

1. A modified neomycin phosphotransferase gene wherein the modified neomycin phosphotransferase gene at amino acid position 91 and/or 198 and/or 240 in relation to the wild-type gene codes for a different amino acid than the wild-type neomycin phosphotransferase gene.

2. The modified neomycin phosphotransferase gene according to claim 1, wherein the modified neomycin phosphotransferase which is encoded by the neomycin phosphotransferase gene has a lower enzyme activity than the wild-type neomycin phosphotransferase.

3. The modified neomycin phosphotransferase gene according to claim 1 wherein the modified neomycin phosphotransferase gene compared with the wild-type gene encodes: alanine at amino acid position 91 and/or glycine at amino acid position 198 and/or isoleucine at amino acid position 240 in relation to the wild-type gene.

4. The modified neomycin phosphotransferase gene according to claim 1 wherein the modified neomycin phosphotransferase gene encodes a polypeptide comprising an amino acid sequence according to SEQ ID NO:6, SEQ ID NO:8 or SEQ ID NO:18.

5. The modified neomycin phosphotransferase gene according to claim 1 comprising a sequence according to SEQ ID NO:5, SEQ ID NO:7 or SEQ ID NO:17.

6. A modified neomycin phosphotransferase gene wherein the modified neomycin phosphotransferase gene compared with the wild-type gene encodes: glycine or aspartic acid at amino acid position 182 and/or alanine or valine or glycine at amino acid position 227 and/or glycine or asparagine at amino acid position 261 in relation to the wild-type gene.

7. The modified neomycin phosphotransferase gene according to claim 6 wherein the modified neomycin phosphotransferase gene encodes a polypeptide comprising an amino acid sequence according to SEQ ID NO:4, SEQ ID NO:10, SEQ ID NO:12 or SEQ ID NO:14.

8. The modified neomycin phosphotransferase gene according to claim 7 comprising a sequence according to SEQ ID NO:3, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13.

9. A modified neomycin phosphotransferase encoded by a modified neomycin phosphotransferase gene according to claim 1.

10. A modified neomycin phosphotransferase encoded by a modified neomycin phosphotransferase gene according to claim 6.

11. A eukaryotic expression vector containing a modified neomycin phosphotransferase gene according to claim 1.

12. A eukaryotic expression vector containing a modified neomycin phosphotransferase gene according to claim 6.

13. A eukaryotic expression vector containing a heterologous gene of interest functionally linked to a heterologous promoter and a modified neomycin phosphotransferase gene which codes for a neomycin phosphotransferase having a lower enzyme activity compared with wild-type neomycin phosphotransferase.

14. A eukaryotic expression vector containing a heterologous gene of interest functionally linked to a heterologous promoter and a modified neomycin phosphotransferase gene which codes for a neomycin

phosphotransferase having a lower enzyme activity compared with wild-type neomycin phosphotransferase wherein:

(i) the modified neomycin phosphotransferase gene is a gene according to claim 1, or

(ii) the modified neomycin phosphotransferase gene at amino acid position 182 and/or 227 codes for a different amino acid than the wild-type gene at the corresponding site, or

(iii) the modified neomycin phosphotransferase gene at amino acid position 261 codes for a glycine.

15. The expression vector according to claim 14, wherein by comparison with the wild-type gene the modified neomycin phosphotransferase gene at amino acid position 182 codes for glycine or aspartic acid and/or by comparison with the wild-type gene the modified neomycin phosphotransferase gene at amino acid position 227 codes for an alanine, glycine or valine.

16. The expression vector according to claim 14, wherein the modified neomycin phosphotransferase gene encodes a protein comprising an amino acid sequence according to SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:18, SEQ ID:20 or SEQ ID NO:22.

17. The expression vector according to claim 14, comprising one or more enhancers functionally linked to the promoter.

18. The expression vector according to claim 17 wherein the enhancer is a CMV or SV40 enhancer.

19. The expression vector according to claim 13 wherein the promoter is a hamster ubiquitin/S27a promoter.

20. The expression vector according to claim 19 wherein the heterologous gene of interest is under the control of the ubiquitin/S27a promoter.

21. The expression vector according to claim 13 further comprising a gene for a fluorescent protein, wherein the gene for the fluorescent protein is, optionally, functionally linked to the gene of interest and the heterologous promoter.

22. The expression vector according to claim 21, further comprising an internal ribosome entry site (IRES), wherein bicistronic expression of the gene which codes for the fluorescent protein and of a gene which codes for a protein/product of interest is enabled.

23. The expression vector according to claim 21, wherein the gene which encodes the fluorescent protein and the gene which encodes the modified neomycin-phosphotransferase gene are located in one or in two separate transcription units.

24. A mammalian cell containing a modified neomycin phosphotransferase gene according to claim 1.

25. A mammalian cell containing a modified neomycin phosphotransferase gene according to claim 6.

26. A mammalian cell which has been transfected with an expression vector according to claim 14.

27. A mammalian cell which has been transfected with an expression vector according to claim 21.

28. The mammalian cell according to claim 27, further transfected with a gene for an amplifiable selectable marker.

29. The mammalian cell according to claim 28, wherein the amplifiable selectable marker gene is dihydrofolate-reductase (DHFR).

30. The mammalian cell according to claim 26, wherein the mammalian cell is a rodent cell.

31. The mammalian cell according to claim 30, wherein the rodent cell is a CHO or BHK cell.

32. A method of enriching a mammalian cell, comprising:

(i) transfecting a pool of mammalian cells with a gene for a modified neomycin-phosphotransferase according to claim 1;

(ii) cultivating the mammalian cells under conditions which allow expression of the modified neomycin-phosphotransferase gene; and

(iii) cultivating the mammalian cells in the presence of at least one selecting agent which acts selectively on the growth of mammalian cells, and gives preference to the growth of the cells which express the modified neomycin-phosphotransferase gene.

33. A method of enriching a mammalian cell, comprising:

(i) transfecting a pool of mammalian cells with a gene for a modified neomycin-phosphotransferase according to claim 6;

(ii) cultivating the mammalian cells under conditions which allow expression of the modified neomycin-phosphotransferase gene; and

(iii) cultivating the mammalian cells in the presence of at least one selecting agent which acts selectively on the growth of mammalian cells, and gives preference to the growth of the

cells which express the modified neomycin-phosphotransferase gene.

34. A method of obtaining and selecting a mammalian cell which expresses at least one heterologous gene of interest, comprising:

(i) transfecting a pool of mammalian cells with at least one gene of interest and a gene for a modified neomycin-phosphotransferase according to claim 1;

(ii) cultivating the mammalian cells under conditions which allow expression of the gene of interest and expression of the modified neomycin-phosphotransferase gene; and

(iii) cultivating the mammalian cells in the presence of at least one selecting agent which acts selectively on the growth of mammalian cells, and gives preference to the growth of the cells which express the modified neomycin-phosphotransferase gene.

35. A method of obtaining and selecting a mammalian cell which expresses at least one heterologous gene of interest, comprising:

(i) transfecting a pool of mammalian cells with at least one gene of interest and a gene for a modified neomycin-phosphotransferase according to claim 6;

(ii) cultivating the mammalian cells under conditions which allow expression of the gene of interest and expression of the modified neomycin-phosphotransferase gene; and

(iii) cultivating the mammalian cells in the presence of at least one selecting agent which acts selectively on the growth of mammalian cells, and gives preference to the growth of the cells which express the modified neomycin-phosphotransferase gene.

36. The method according to claim 34, further comprising transfecting the mammalian cells with a gene for an amplifiable selectable marker and subjecting the selected mammalian cells to at least one gene amplification step, wherein the amplifiable selectable marker gene encodes dihydrofolate-reductase (DHFR), and wherein the gene amplification is carried out by the addition of methotrexate.

37. The method according to claim 35, further comprising transfecting the mammalian cells with a gene for an amplifiable selectable marker and subjecting the selected mammalian cells to at least one gene amplification step, wherein the amplifiable selectable marker gene encodes dihydrofolate-reductase (DHFR), and wherein the gene amplification is carried out by the addition of methotrexate.

38. A method of obtaining and selecting a mammalian cell which expresses at least one heterologous gene of interest, comprising:

(i) transforming recombinant the mammalian cell with an expression vector according to claim 21;

(ii) cultivating the recombinant mammalian cell under conditions which allow expression of the gene of interest and expression of the gene which codes for a fluorescent protein, and expression of the modified neomycin-phosphotransferase gene;

(iii) cultivating the mammalian cell in the presence of at least one selecting agent which acts selectively on the growth of the mammalian cell, and gives preference to the growth of the cells which expresses the modified neomycin-phosphotransferase gene; and

(iv) sorting the mammalian cell which expresses at least one heterologous gene of interest by flow-cytometric analysis.

39. The method according to claim 39, wherein that the mammalian cell is additionally transfected with a gene for an amplifiable selectable marker

and the cell of step (iv) which is sorted by flow-cytometric analysis is subjected to at least one gene amplification step, wherein the amplifiable selectable marker gene is dihydrofolate-reductase (DHFR), and wherein the gene amplification is carried out by the addition of methotrexate.

40. A method of producing at least one protein of interest in a recombinant mammalian cell, comprising:

(i) transfecting a pool of mammalian cells with at least one gene of interest and one gene for a modified neomycin-phosphotransferase according to claim 1;

(ii) cultivating the cell under conditions which allow expression of the gene of interest and of the modified neomycin-phosphotransferase;

(iii) cultivating the mammalian cell in the presence of at least one selecting agent which acts selectively on the growth of the mammalian cell, and gives preference to the growth of the cell which expresses the modified neomycin-phosphotransferase gene; and

(iv) obtaining the protein of interest from the mammalian cells or the culture supernatant.

41. A method of producing at least one protein of interest in a recombinant mammalian cell, comprising:

(i) transfecting a pool of mammalian cells with at least one gene of interest and one gene for a modified neomycin-phosphotransferase according to claim 6;

(ii) cultivating the cell under conditions which allow expression of the gene of interest and of the modified neomycin-phosphotransferase;

(iii) cultivating the mammalian cell in the presence of at least one selecting agent which acts selectively on the growth of the mammalian cell, and gives preference to the growth of the cell

which expresses the modified neomycin-phosphotransferase gene; and

(iv) obtaining the protein of interest from the mammalian cells or the culture supernatant.

42. A method of producing at least one protein of interest in a recombinant mammalian cell, comprising:

(i) transforming the recombinant mammalian cell with an expression vector according to claim 21;

(ii) cultivating the cell of step (i) under conditions which allow expression of the gene of interest, expression of the gene which codes for a fluorescent protein, and expression of the modified neomycin-phosphotransferase gene;

(iii) cultivating the mammalian cell in the presence of at least one selecting agent which acts selectively on the growth of the mammalian cell, and gives preference to the growth of the cell which expresses the modified neomycin-phosphotransferase gene;

(iv) sorting the mammalian cell by flow-cytometric analysis; and

(v) obtaining the protein of interest from the mammalian cell or the culture supernatant.

43. A method of producing at least one protein of interest, comprising:

(i) cultivating the mammalian cell according to claim 28 under conditions which allow expression of the gene of interest, expression of the modified neomycin-phosphotransferase gene and expression of the amplifiable selectable marker gene;

(ii) cultivating the mammalian cell and selecting the mammalian cell in the presence of at least one selecting agent which acts selectively on the growth of the mammalian cell, and gives preference to the growth of the cell which expresses the modified neomycin-phosphotransferase gene;

(iii) subjecting the selected mammalian cell to at least one gene amplification step; and

(iv) obtaining the protein of interest from the mammalian cell or the culture supernatant.

44. The method according to claim 40, comprising:

(i) transfecting the mammalian cells with at least two genes of interest which code for a heteromeric protein/product,

(ii) cultivating the mammalian cells under conditions which allow expression of the subunits of the heteromeric protein/product; and

(iii) isolating the heteromeric protein/product from the culture or culture medium.

45. The method according to claim 44, wherein an average specific productivity of the sorted mammalian cells is more than 5pg of the desired gene product per day per cell.

46. The method according to claim 41, wherein the average specific productivity is more than 20pg of the desired gene product per day per cell.

47. The method according to claim 34, wherein the mammalian cell is a rodent cell.

48. The method according to claim 47, wherein the rodent cell is a CHO or BHK cell.

49. The method according to claim 34, wherein the mammalian cells are cultivated in suspension culture.

50. The method according to claim 34, wherein the mammalian cells are cultivated in a serum-free culture medium.

51. The method according to claim 35, wherein the mammalian cell is a rodent cell.

52. The method according to claim 51, wherein the rodent cell is a CHO or BHK cell.

53. The method according to claim 35, wherein the mammalian cells are cultivated in suspension culture.

54. The method according to claim 35, wherein the mammalian cells are cultivated in a serum-free culture medium.